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Document history					
Version #	**Status (I, R, C)**	**Date Approved**	**Location of Change History**	**Name & Title**	
				Contact	**Approving Official**
1.0	I	November 21, 2005	In Document	James Allgire	Lucinda F. Buhse

Chronologically track the original document and/or approved revisions or cancellations.

(a) Version # of the Document
(b) Status: I = Initial; R = Revision; C = Cancel
(c) Date Approved by the Approving Official
(d) Location of the Change History
(e) Name, Title of Contact/Approving Official: Include the organization abbreviation in the title. The contact may or may not be the author.

1. Purpose

The purpose of this document is to establish the set-up, mechanical calibration, and operation checks for dissolution Apparatus 1 and 2.

2. Scope/Policy

This procedure applies to all Apparatus 1 and 2 dissolution equipment at the Division of Pharmaceutical Analysis (DPA).

3. Responsibilities

3.1 Analyst

- Check the vessel, basket, and paddle dimensions on receipt.
- Perform the maintenance procedures on receipt and every six months. If the instrument is not being used routinely the six month maintenance procedure can be performed before performing the first dissolution test after the six month time interval.
- Perform the mechanical calibration on receipt, after the instrument is moved, after the instrument is repaired, and six months after the previous calibration. If the instrument is not being used routinely the six month mechanical calibration can be performed before performing the first dissolution test after the six month time interval.
- Perform the operation checks at each time of use.

4. Background

The set-up, mechanical, and operational checks are used to minimize variability during dissolution testing.

5. References

- USP General Chapter <711>
- <1092> The Dissolution Procedure: Development and Validation, Pharmacopeial Forum, 30(1), (2004), pp.351-363
- JAMA, 182(12), (1962), pp.1146-1154

6. Procedure

Wherever possible, tools should be traceable to NIST.

6.1 Apparatus set-up

During apparatus set-up or after replacement of parts, verify the following. Discard any parts that do not meet specifications:

Vessel Dimensions

A 6 inch digital caliper is used to verify that most dimensions conform to the specifications listed in the USP General Chapter <711> Dissolution. A ruler is used to measure the vessel height. The bottom of each vessel must be felt with your fingertips and if any deformities, such as indentations or bumps in the smooth surface are found, the vessel must be discarded.

Basket Dimensions

Each basket must conform to the dimensions shown in the USP General Chapter <711> Dissolution in Figure 1, Basket Stirring Element. A digital caliper is used to make the measurements.

Paddle Dimensions

Each paddle must conform to the dimensions shown in the USP General Chapter <711> Dissolution in Figure 2. A digital caliper is used to make the measurements.

6.2 Maintenance

Visual Inspection of Belts, Check Ball Bearings

During the apparatus set-up and every six months thereafter, if applicable for the particular dissolution apparatus, remove the cover of the drive module and loosen the belts. Turn each shaft manually and feel if it rotates smoothly. If any do not rotate smoothly, the ball bearings may be worn or damaged and need to be replaced. For routine maintenance, place a drop of oil on each of the bearings and rollers. Replace the belts and check to see if they are clean, free of cracks and properly aligned. If the instrument is not in routine use, the maintenance procedure may be performed prior to performing the first dissolution test after the six month interval.

6.3 Mechanical Calibration

Perform the following in the order given for mechanical calibration of each apparatus. Perform these tests every 6 months or after repair/move/etc. If the instrument is not in routine use, the mechanical calibration may be performed prior to performing the first dissolution test after the six month interval.

Shaft Wobble

Use a Distek wobble meter or equivalent. The meter is set on top of the base plate, and the drive module is positioned so that the gauge probe touches the shaft about 2 cm above the top of the paddle blade or basket. The shaft RPM is set to 50. The gauge is placed so that the probe slightly presses in on the turning shaft. The gauge's pointer should read slightly more than zero. The pointer will vary from a minimum to a maximum reading and the difference is called the wobble. The DPA limit is less than or equal to 0.5 mm total runout. If the reading is larger, the shaft may be bent and will have to be discarded or sent to the manufacturer to be straightened. Another problem could be that the bearings in the drive module are worn making the shafts loose.

Basket Wobble

A wobble meter is set on top of the base plate and the drive module is positioned so that the gauge probe touches the bottom rim of the basket. The shaft RPM is set to 50. The gauge is placed so that the probe slightly presses in on the turning shaft. The gauge's pointer should read slightly more than zero. The pointer will vary from a minimum to a maximum reading and the difference is called the wobble. The DPA tolerance is ≤ 1.0 mm total runout. If the reading is larger, the basket sides may not be vertical. The bottom of the basket can be pushed sideways to straighten the sides of the basket. This procedure is repeated until the basket wobble is within tolerance.

Paddle and Basket Shaft Verticality

Lower the drive module where it would be during an actual dissolution test. Place a bubble level on the front edge of each of the shafts. The bubble should be centered within the lines of the level. Rotate the level 90º so it is on the side of the shaft. The bubble should again be centered within the lines of the level for each shaft. If the shafts are not vertical adjust the feet of the apparatus until they are vertical.

Vessel Centering / Vessel Verticality

Sometimes the base plate of an apparatus will warp or bend or the thickness of a vessel lip or centering collar lip may not be perfectly uniform. If this occurs, even if the shafts are vertical and the base plate is level, the vessel walls may not be vertical. Most vessel centering devices measure centering inside the lip of the vessel where deformities in the vessel may occur which can prevent accurate centering of the vessel. DPA uses a vessel centering / verticality procedure that overcomes these problems.

The Distek CenterChek centering tool measures centering inside the vessel. Two Distek CenterChek centering tools are used to center the vessels around the paddle or basket shafts and to align the vessels so that their sides are vertical. For the paddle method, the bottom of one centering tool is placed 1.5 mm above the top of the paddle blade and the bottom of the second centering tool is clamped on the shaft 80 mm above the blade with the probes positioned in the same direction towards the glass vessel wall. For the basket method, the bottom of one centering tool is placed 1.5 mm above the top of the basket and the bottom of one centering tool is placed 60 mm above the top of the basket. Carefully lower the shaft and CenterChek tools into the vessels so that the paddle blade or basket bottom is about 2.5 cm above the bottom of the vessel. The first centering tool position is near the 300ml level when using the paddle and the 450 ml level when using the basket. The second centering tool is near the 900 ml level. Manually slowly turn the shaft and check the centering at both levels. If the vessel is not centered on either level, adjust the vessel to make it centered. Adjustments can be made by rotating the vessel or the vessel with the centering collar inside the base plate, moving the vessel sideways within the base plate or placing shims (such as tape) under one side of the lip of the vessel or vessel centering collar. Repeat this process until both bottom and top positions are centered within 1mm tolerance.

If only one centering tool is available, first place the bottom of the CenterChek 1.5 mm above the top of the paddle or basket and lower the shaft into the vessel so that the bottom of the paddle blade or basket is about 2.5 cm above the vessel bottom. Center the vessel, then move the centering tool so that the bottom of the tool is 80 mm above the top of the paddle or 60 mm above the top of the basket and check the second level centering. If the vessel is not centered on the second level, adjust the vessel to make it centered. Repeat this process until both bottom and top positions are centered within the 1mm tolerance.

After each vessel has been centered and made vertical, each vessel and baseplate opening must be numbered and a mark must be placed on the lip of each vessel and on the baseplate directly next to the mark on the vessel lip. Each vessel must be returned to the same baseplate opening and positioned in the exact same position inside the baseplate opening for all future dissolution tests.

Basket and Paddle Depth
A Distek HeightChek tool is used to set the distance between the bottom of the paddle blade or basket and the bottom of the vessel. The HeightChek is set at 25 mm and placed on the bottom of the vessel. The height adjustment collar on each shaft is loosened and each shaft raised into the apparatus head. The apparatus head is then lowered until it touches the height adjustment spacer block for paddles. Do not use the height adjustment spacer block for baskets. The paddle or basket is then lowered into the vessel until it touches the top of the HeightChek tool. The height adjustment collar is lowered so it is resting on the top of the Teflon spindle around that shaft and then the collar is tightened to the shaft. This is repeated for each shaft.

Vibration
The USP criteria of: "No part of the assembly, including the environment in which the assembly is placed, contributes significant motion, agitation, or vibration beyond that due to the smoothly rotating stirring element" is followed.

Rotational Speed
An optical digital tachometer should be used to measure the rotational speed of the paddle or basket. The DPA limit is ± 2 rpm.

6.4 Operation

Before each run perform the following:

Basket Examination
Each basket must be visually examined for defects such as rusting, the edge of the wire mesh sticking out beyond the basket, clogged mesh holes and smashed in mesh sides.

Paddle Examination
Each paddle must be visually examined for defects such as rusting and loose pieces of coating sticking out from the paddles (for paddles coated with Teflon or another coating).

Vessel Temperature
The temperature of the medium inside each vessel is measured at time of use. The limit is 37 ± 0.5% C.

6.5 Additional Variables

Basket Shafts (Clips verses O rings)
The diagram of the basket stirring element in the USP General Chapter <711> shows that the basket shaft has clips to hold the basket. Distek Inc. makes basket shafts that have O rings to hold the basket in place instead of clips. The clips change the hydrodynamics of the medium causing slightly increased dissolution results with certain formulations. In order to conform to the USP diagram, DPA chemists must use the detachable snap on basket clips from Distek.

Sinkers
Sinkers are required for capsules that float when the paddle method is used. Some commercial sinkers have too many coils that trap the capsule material inside the sinker. DPA uses sinkers that are recommended by the USP. A detailed procedure on how to make them is in the proposed USP General Chapter <1092> The Dissolution Procedure: Development and Validation, USP Pharmacopeial Forum, 30(1), 2004, pp. 353 in the Pharmacopeial Previews section. If a method states to use a particular commercially available sinker, the chemist must use the specified sinker.

7. **Records**
   The date, analyst, glass dissolution vessels manufacturer, and the dissolution apparatus's manufacturer, model number, and serial number will be recorded on the appropriate Mechanical Calibration Report Sheet (see Attachment B and C) along with the appropriate observations. The completed report sheet will be placed in the report sheet folder for that apparatus. Each dissolution apparatus will have its own report sheet folder.

8. **Glossary**
   Not Applicable

9. **Attachments**
   Attachment A - Sinkers
   Attachment B - Mechanical Calibration Report Sheet--Apparatus 1 (Basket)
   Attachment C - Mechanical Calibration Report Sheet--Apparatus 2 (Paddle)

Signatures
Approving Official's Signature:

_____ _____
Benjamin J Westenberger, Deputy Director Date

_____ _____
Lucinda F Buhse, Director Date

Attachment A

Sinkers

"As a guide, the following is a suggested procedure for making sinkers by hand.
Materials: 316 stainless steel wire, 0.032 inch/20 gauge; one set of cork borers #1 to #15.

Capsule Shell	Cork Bore	Length of Wire in inches (cm)	Diameter Size in inches (cm)
0, elongated	#4	4.72 (12)	0.313 (0.8)
1 and 2	#3	3.94 (10)	0.275 (0.7)
3 and 4	#2	3.15 (8)	0.215 (0.55)

Procedure— Cut the specified length of coil length wire around the specified bore of the appropriate size, and use small pliers to curve in the ends. In countries where normal values for wire diameters vary from the tabulated values, use wire with the nearest metric dimension.

There are commercially available sinkers that, if properly validated, may be used. The type of sinker should always be clearly defined in the procedure or test method. If the sinker is handmade, the sinker construction procedure instructions should be documented. If a commercial sinker is used, the vendor specifications should be defined."

(<1092> The Dissolution Procedure: Development and Validation, Pharmacopeial Forum, 30(1), (2004), pp.353)